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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,924	10/31/2000	Hiroyoshi Hidaka	198323US0PCT	6890

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,924	HIDAKA ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-16* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-13,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's response filed 8/26/2004 is acknowledged and entered.

2. Claim 3 was canceled and Claims 5, and 14 were amended by the amendment filed on 3/1/2004.

3. Claims 2, and 4 are canceled, and claims 15-16 are added by the amendment filed on 6/30/03.

4. Claim 1 is canceled, and claims 5-14 are added by the amendment filed on 5/8/02.

5. Claims 5-16 are pending.

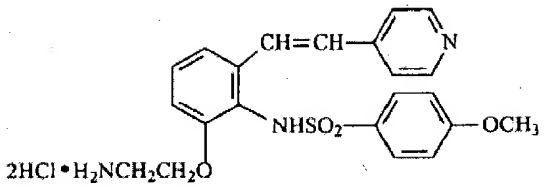
Election/Restrictions

6. Applicant has elected the following species for the elected invention (Claims 5-16):

   a. A species of antigenic substance is serum albumin.

   b. A species of chemical cross-linker is glutaraldehyde.

   c. A species of drug is drug A, which has the following structure:



7. Claim 14 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***a nonelected species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed 8/30/02 and 10/9/02.

Priority

8. This application is a 371 of PCT/JP98/01712 filed 4/15/1998.

9. Claims 5-13, and 15-16 are treated on the merit in this Office Action.

Maintained Rejections

Claim Rejections - 35 USC § 103

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

11. Claims 5-10, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22.

Gram et al. disclose a method for *in vitro* detection of a gene encoding a drug-targeted protein (Abstract; pg. 3578, left col., line 19 to right col. line 4). The method comprises the phage displaying low affinity Fabs binding to a progesterone-bovine serum albumin conjugate (drug-serum albumin) were isolated from the library (pg. 3578, left col., line 19 to right col. line 4; pg. 3577, left col., lines 44-62). The drug-targeted protein comprise of progesterone-bovine serum albumin wherein the progesterone bind to the bovine serum albumin via a linker comprising 3-(*O*-carboxymethyl) oxime (pg. 3577, left col., lines 47-48). The phage display comprises *Escherichia coli* (pg. 3577, left col., lines 39-43) (refers to claims 6 and 15). The library comprises murine cDNA expression library (pg. 3577, left col., lines 1-34) (refers to claim 7). Additionally with regards to claims 8-10, the type of cDNA expression library would be a choice of experimental design and is considered within the purview of the cited prior art.

The method of Gram et al. does not expressly include the chemical cross-linker such as glutaraldehyde as the linker that couples the drug to the antigenic substance.

Pecht et al. disclose the method of forming a drug-BSA conjugate (col. 4, lines 13-26). The method comprises using glutaraldehyde as a bifunctional reagent to couple the drug to BSA (bovine serum albumin).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the chemical cross-linker such as glutaraldehyde as the linker that couples the drug to the antigenic substance as taught by Pecht et al. in the method of Pecht et al. One of ordinary skill in the art would have been motivated to include the chemical cross-linker such as glutaraldehyde as the linker that couples the drug to the antigenic substance in the method of Gram et al. because the type linker use to couple the drug to an antigenic substance

would be a choice of experimental design and is considered within the purview of the cited prior art. Furthermore, one of ordinary skill in the art would have reasonable expectation of success in the teaching of Gram et al. and Pecht et al. because both disclose using a drug-BSA conjugate to bind to an antibody (Gram: pg. 3578, right col., lines 1-4; Pecht: col. 4, lines 49-68).

Additionally, the instant specification on page 3 discloses that"[N]o particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance" (lines 19-22). Thus it would be obvious to one skilled in the art to use different type of bifunctional linkers to couple the drug to an antigenic substance such that it would be a choice of experimental design.

12. Claims 11-12, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580) Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 as applied to claims 5-10, and 15 above, and further in view of Barbas III et al. (*Proc. Natl. Acad. Sci. USA*, **1991**, 88:7978-7982).

Gram et al. disclose a method for *in vitro* detection of a gene encoding a drug-targeted protein (Abstract; pg. 3578, left col., line 19 to right col. line 4). The method comprises the phage displaying low affinity Fabs binding to a progesterone-bovine serum albumin conjugate (drug-serum albumin) were isolated from the library (pg. 3578, left col., line 19 to right col. line 4; pg. 3577, left col., lines 44-62). The phage display comprises *Escherichia coli* (pg. 3577, left col., lines 39-43) (refers to claims 6 and 15). The library comprises murine cDNA expression library (pg. 3577, left col., lines 1-34) (refers to claim 7). Additionally with regards to claims 8-10, the type of cDNA expression library would be a choice of experimental design and is

considered within the purview of the cited prior art. Both Gram et al. and Pecht et al. disclose using a drug-BSA conjugate to bind to an antibody (Gram: pg. 3578, right col., lines 1-4; Pecht: col. 4, lines 49-68). Gram et al. disclose drug-targeted protein comprise of progesterone-bovine serum albumin, wherein the progesterone bind to the bovine serum albumin via a linker comprising 3-(*O*-carboxymethyl)oxime. Pecht et al. disclose the method of forming a drug-BSA conjugate wherein glutaraldehyde is used as a bifunctional reagent to couple the drug to BSA (bovine serum albumin) (col. 4, lines 13-26).

Additionally, the specification on page 3 stated that"[N]o particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance" (lines 19-22). Thus, the type of linker use to couple the drug to BSA would be a choice of experimental design and is considered within the purview of the cited prior art.

The combination of Gram et al. and Pecht et al. does not expressly include employing a membrane to capture phage from plated phage culture.

Barbas III et al. disclose a method of colony screening of panned libraries (pg. 7979, right col., lines 12-27). The method comprises using nitrocellulose filters (membrane) with isopropyl β-D-thiogalactopyranoside to capture the phage from plated phage culture (pg. 7979, right col., lines 12-16) (refers to claims 11-12, and 16).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include employing a membrane to capture phage from plated phage culture as taught by Barbas III et al. in the method of Gram et al. and Pecht et al. One of ordinary skill in the art would have been motivated to include employing a membrane to capture

phage from plated phage culture in the method of Gram et al. and Pecht et al. because Gram et al. incorporated the method of Barbas III et al. by reference into the disclosed colony screening method of panned libraries (Gram: pg. 3577, left col., lines 57-60). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Gram et al., Pecht et al., and Barbas III et al. because Gram et al. uses Barbas III et al. colony screening method of panned libraries (Gram: pg. 3577, left col., lines 57-60).

Response to Arguments

13. Applicant's arguments directed to the rejection under 35 USC 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580), Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 for claims 5-10, and 15 were considered but they are not persuasive for the following reasons.

Applicant alleges that the combination of Gram et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 is not obvious over the presently claimed method because 1) "*Although the Examiner cites this reference for disclosing a method for in vitro detection of a gene encoding a drug-targeted protein, Applicants disagree*"; 2) "*Applicants note that at no point do Gram et al disclose or suggest that their progesterone-bovine serum albumin conjugate is used to detect genes of the target protein in a living body*"; 3) "*The methods of Gram et al are limited to phage display methods*"; 4) there is no motivation to combine the references of Gram et al., and Pecht et al. because "*the bifunctional reporters disclosed by Pecht et al are for immunoprecipitation methods*". Thus the combination of Gram et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 is not obvious over the presently claimed method.

Applicant's arguments are not convincing since the combination of Gram et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 is obvious over the presently claimed method. It is the examiner position that:

1) Applicant's argument, i.e. "*Although the Examiner cites this reference for disclosing a method for in vitro detection of a gene encoding a drug-targeted protein, Applicants disagree*", fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

2) In response to applicant assertion that "*at no point do Gram et al disclose or suggest that their progesterone-bovine serum albumin conjugate is used to detect genes of the target protein in a living body*", it is noted that the presently claimed method recite a method for *in vitro* detection. The term "*in vitro*" as define by the Webster's Dictionary as in an artificial environment outside the living organism. Thus applicant assertion is contradictory to the presently claimed method for it support that Gram et al. disclose a method for *in vitro* detection as claimed by the presently claimed method.

3) In response to applicant argument that "*The methods of Gram et al are limited to phage display methods*", it is noted that the presently claimed method does not exclude the method of phage display in fact the presently claimed method claimed the method of phage display. Claim 6 recites "*The method of claim 15, wherein said phage display method employs Escherichia coli as a host cell.*" Claim 15 recites "*The method of claim 5, wherein said expressed is by phage display method.*" Thus the presently claimed method includes the method of phage display as disclosed by Gram et al.

4) In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, a) both Gram et al. and Pecht et al. disclose using a drug-BSA conjugate to bind to an antibody, i.e. analogous art, (Gram: pg. 3578, right col., lines 1-4; Pecht: col. 4, lines 49-68), and b) the specification on page 3 stated that"[N]o particular limitation is imposed on the chemical cross-linkers so long as they provide a group which cross-links a functional group of the drug and a functional group of the antigenic substance" (lines 19-22). Thus, the type of linker use to couple the drug to BSA would be a choice of experimental design and is considered within the purview of the cited prior art.

Thus, the combination of Gram et al., Pecht et al., and the specification disclosure on page 3, lines 19-22 is obvious over the presently claimed method, and the rejection is maintained.

14. Applicant's argument directed to the rejection under 35 USC 103(a) as being unpatentable over Gram et al. (*Proc. Natl. Acad. Sci. USA*, **1992**, 89:3576-3580) Pecht et al. (US Patent 4,683,135), and the specification disclosure on page 3, lines 19-22 as applied to claims 5-10, and 15 above, and further in view of Barbas III et al. (*Proc. Natl. Acad. Sci. USA*, **1991**,

88:7978-7982) for claims 11-12, and 16 were considered but they are not persuasive for the following reasons.

Applicant contends that the combination of Gram et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. is not obvious over the presently claimed method because the combine disclosures of Gram et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. "*fail to compensate for the basic deficiency in the disclosure of Gram et al.*", which are 1) "*Although the Examiner cites this reference for disclosing a method for in vitro detection of a gene encoding a drug-targeted protein, Applicants disagree*"; 2) "*Applicants note that at no point do Gram et al disclose or suggest that their progesterone-bovine serum albumin conjugate is used to detect genes of the target protein in a living body*"; 3) "*The methods of Gram et al are limited to phage display methods*". Therefore, the combination of Gram et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. is not obvious over the presently claimed method.

Applicant's arguments are not convincing since the combination of Gram et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. is obvious over the presently claimed method because Gram et al. does not lack "*the basic deficiency*". It is the examiner position that:

1) Applicant's argument, i.e. "*Although the Examiner cites this reference for disclosing a method for in vitro detection of a gene encoding a drug-targeted protein, Applicants disagree*", fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references.

2) In response to applicant assertion that "*at no point do Gram et al disclose or suggest that their progesterone-bovine serum albumin conjugate is used to detect genes of the target protein in a living body*", it is noted that the presently claimed method recite a method for *in vitro* detection. The term "*in vitro*" as define by the Webster's Dictionary as in an artificial environment outside the living organism. Thus applicant assertion is contradictory to the presently claimed method for it support that Gram et al. disclose a method for *in vitro* detection as claimed by the presently claimed method.

3) In response to applicant argument that "*The methods of Gram et al are limited to phage display methods*", it is noted that the presently claimed method does not exclude the method of phage display in fact the presently claimed method claimed the method of phage display. Claim 6 recites "*The method of claim 15, wherein said phage display method employs Escherichia coli as a host cell.*" Claim 15 recites "*The method of claim 5, wherein said expressed is by phage display method.*" Thus the presently claimed method includes the method of phage display as disclosed by Gram et al.

Thus the combination of Gram et al., Pecht et al., the specification disclosure on page 3, lines 19-22, and Barbas III et al. is obvious over the presently claimed method, and the rejection is maintained.

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
November 5, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER